Previously, Applicants respectfully submitted that in the device illustrated in Fig. 4 of Weigl et al, one reads in col. 23, lines 22 – 32 of Weigl et al that sample stream 2 contains large particles, medium-sized particles, and small particles. Sample stream 2 meets with an extraction stream 4 to form a laminar flow in extraction channel 7 in Weigl et al. In extraction channel 7, small particles with larger diffusion coefficients, which diffuse most rapidly in the lateral direction towards first product outlet channel 24, exit the device through first product outlet 23 in Weigl et al.

Previously, Applicants respectfully directed the Examiner's attention to the fact that the first product outlet channel 24, like all the additional product outlet channels seen in Fig. 4 of Weigl et al, has a diameter much larger than the diameter of all the particles involved. That means, all particles, i.e. large particles, medium-sized particles, or small particles, that find their way to the entrance of any product outlet channel are allowed to pass through this channel. In other words, it is not the product outlet channels that are designed so as to perform the size-oriented particle selection or sorting process. Instead, and in sharp contrast to the Applicants' invention, it was noted that it is the difference in lateral diffusion velocity of the different particles within the sample stream in extraction channel 7 in Weigl et al, that results in the "addressing" of particular product outlet channels out of a multitude of product outlet channels of equal dimensions. Since the lateral diffusion velocity is related to the particles size (see Weigl et al, col. 22, lines 13 – 37) different classes of particles according to their size will "address" different product outlet channels.

Previously, Applicants respectfully submitted that Applicants' comments are also supported by the following statements that can be found in Weigl et al, col. 23, lines 33 – 43: "Medium-sized particles with medium-range diffusion coefficients exit along with small particles through second product outlet 26 in second exiting product stream 28 through second product outlet channel 27 placed further from sample stream inlet 1 than first product outlet channel 24 so as to allow more time for medium-sized particles to diffuse into the extraction stream. Large particles which have smaller diffusion coefficients and which diffuse more slowly exit third product outlet 29 in third

exiting product stream 31 through third product outlet channel 30, along with small and medium-sized particles."(Emphasis added) These statements in Weigl et al demonstrate that whatever particles are arriving at the entrance of any of the product outlet channels will pass through. It was pointed out that one can also observe from these statements in Weigl et al that the separation effect for particles of different size is not perfect in a device according to Weigl et al. In Applicants' invention all of the larger particles will be held back, and the separation is perfect.

Applicants noted that the device of Weigl et al has output channels for receiving and passing through of particles of any size. Size-separation is achieved by taking advantage of a fluid-dynamic process wherein the particle size has an impact on the fluid dynamics so that particles of different size are arriving at equal output channels that are positioned at different locations. In Applicants' invention, the channel structure is so designed that particles of interest are held back, and therefore "concentrated", at the entrance of the channels. Consequently, Applicants respectfully submitted that it would not have been obvious to utilize the teachings of Weigl et al to use output channels with diameters much larger than particles of interest in order to concentrate such particles.

In his response to Applicants' above arguments filed in the Amendment dated December 4, 2003, the Examiner contends that these arguments have been fully considered, but that they are not persuasive. After carefully studying the present Official Action, Applicants respectfully submit the following additional comments to delineate the essential differences between the device according to Weigl and the present invention.

First, the Examiner's attention is directed to col. 14, lines 23-26 of Weigl, where it is taught that "successful operation of the inventions described herein requires precise control of volume flow rates on three of the four channels of the device (i.e. sample, extraction, product, and by-product streams)." Second, in col. 40, lines 9-13, Weigl discloses that "These microfluidic devices of this invention require laminar, non-turbulent flow and are designed according to the foregoing principles to produce flows

having low Reynolds numbers, preferably below about 1, e.g., below 0.1." Third, in col. 49, claim 10, Weigl discloses "The microfluidic system of claim 1 wherein said means for controlling fluid flow are pressure control means."

The first of the above citations clearly indicates that a device according to Weigl has and needs at least four flow channels for guiding streams. In order for the device to function, the sample stream and the extraction stream are flowing parallel to each other within one chamber so that diffusion of particles from one stream into the other can take place. As the second citation states, a laminar non-turbulent flow pattern is required for these streams, which is achieved by controlling the volume flow rate in three of the four channels properly by means of pressure control means. In other words, the flow speed in the sample stream and in the extraction stream have to be equal to avoid turbulence-causing friction at the joint interface, and have to be properly low to maintain a low Reynolds number, allowing for a laminar flow pattern. If all of these complex conditions are fulfilled and maintained, effective diffusion of smaller particles from the sample stream into the extraction stream will occur, which is a partial goal for a device according to Weigl.

In contrast to a device according to Weigl, the present invention does not have at least four channels and streams, but has only one broad channel comprising a wall with openings, and this wall is oriented perpendicular to the main flow direction. Moreover, the present invention does not require special attention for controlling the volume flow rate. The liquid sample enters the device through a sample entrance and flows towards the end of the device, whereby no specific flow speed or specific Reynolds number are required. Consequently, the present invention does not need and does not have any control means for controlling the volume flow rate. There is no need for achieving and maintaining a laminar flow pattern. All that is needed is an even flow front, which is achieved by means of a plurality of notches. These notches allow for temporary flow components perpendicular to the main flow direction to even out the overall flow front, which is not a laminar flow pattern.

Applicants had noted in their earlier arguments filed December 4, 2003 that in Weigl size-separation is achieved by taking advantage of a fluid-dynamic process wherein the particle size has an impact on the fluid dynamics so that particles of different size are arriving at output channels that are positioned at different locations. In the present invention, however, the channel structure is so designed that particles of interest are held back, and therefore "concentrated", at the entrance of through channels in a separation wall. In other words, while in a device according to Weigl particle separation is achieved by means of a fluid-dynamic process, separation is achieved in the device of the present invention by means of "hardware" in the form of a wall containing properly sized through channels, whereby fluid-dynamic processes are not coming into play.

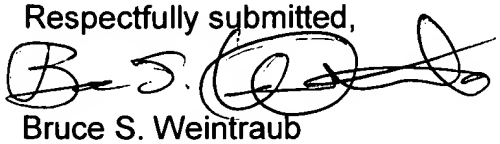
Applicants respectfully submit that considering the additional arguments together with Applicants' earlier arguments filed December 4, 2003 clearly demonstrates that it would not have been obvious to one of ordinary skill in the art to just modify the channels taught in Weigl to isolate larger particles in lieu of smaller particles if the desired end result was to capture larger particles.

Withdrawal of the present rejection under Section 103(a) is respectfully requested.

Applicants again note with appreciation that the Examiner has found Claims 9-12 and 15-18 to be allowable if rewritten in independent form.

In view of the above Remarks, it is believed that all of the claims of the present application are believed to be in condition for allowance. Early notice thereof is respectfully requested by Applicants.

Respectfully submitted,



Bruce S. Weintraub
Attorney for Applicants
Registration No. 34,277

Becton Dickinson and Company
1 Becton Drive
Franklin Lakes, New Jersey 07417
(201) 847-7096

#79831